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(54) Title: METHOD AND COMPOSITION FOR TREATING MUCO-EPIDERMAL AND EPIDERMAL PAIN, INFLAMMATION AND INFECTION

(57) Abstract

A topical pharmaceutical preparation for the treatment of epidermal and muco-epidermal tissue is provided. The composition includes a therapeutic amount of chlorexidine and at least one non-steroidal anti-inflammatory agent. A method for treating epidermal and muco-epidermal pain, inflammation, infection and lesion by applying the topical preparation directly to the affected site is also provided.

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METHOD AND COMPOSITION FOR TREATING MUCO-EPIDERMAL AND EPIDERMAL PAIN, INFLAMMATION AND INFECTION

BACKGROUND OF THE INVENTION

The present invention relates generally to pharmaceutical preparations for the treatment of muco-epidermal and epidermal tissue. More particularly, the present invention relates to gels, creams, solutions and other topical preparations including a mixture of chlorhexidine and at least one non-steroidal anti-inflammatory agent. The invention further provides a method for the treatment of muco-epidermal and epidermal tissue using such preparations.

The antimicrobial effects of chlorhexidine are well-documented. Chlorhexidine gels, rinses and creams are routinely used to control bacterial infections on mucosal epidermal and epidermal tissue. For example, chlorhexidine gels and rinses are widely used in dentistry for the treatment of periodontal disease. Non-steroidal anti-inflammatory agents such as ibuprofen, ketoprofen and indomethacin have application in the treatment of, for example, inflammatory diseases such as arthritis, general muscle, skeletal and joint pain and menstrual cramps.

While these compounds have been widely used individually by physicians and dentists in the above-described manner for many years, the effectiveness of a combination of chlorhexidine and a non-steroidal anti-inflammatory agent has not been appreciated.

Accordingly, it is the object of the present invention to provide a pharmaceutical preparation including a combination of chlorhexidine and at least one anti-inflammatory agent which together show a synergistic effect in the treatment of muco-epidermal and epidermal inflammation and infection.

It is a further object of the invention to provide a method for treating muco-epidermal and epidermal tissue using such preparations.

SUMMARY OF THE INVENTION

The present invention meets the above-stated objects and others that will become readily apparent by providing topical pharmaceutical preparations which include chlorhexidine and at least one non-steroidal anti-inflammatory agent. These active ingredients are incorporated into a gel, cream, solution, rinse or other pharmaceutically acceptable carrier and are applied topically to sites of epidermal and muco-epidermal inflammation, infection or lesion.

The preparations which are the subject of the present invention include a non-toxic amount of chlorhexidine and preferably include, as the non-steroidal anti-inflammatory agent, indomethacin, ibuprofen, ketoprofen or other prostaglandin inhibitors.

As demonstrated below by the various examples provided, the combination of chlorhexidine and a non-steroidal anti-inflammatory agent unexpectedly show a synergistic effect in the treatment of a number of conditions including, periodontal disease, acne, post-radiation therapy, post-chemotherapy therapy, post-surgical therapy, burns and non-specific epidermal and muco-epidermal infections.

The present invention is also directed to a method for treating epidermal and muco-epidermal tissue employing the above-described topical preparations. The course of therapy with such preparations generally requires one to three applications per day or is applied on an as needed basis, depending on the severity of the condition. Treatment includes directly applying the topical preparations to the affected site.

DETAILED DESCRIPTION OF THE INVENTION

As noted above, the-topical pharmaceutical preparations of the present invention include chlorhexidine in a therapeutically effective amount. For most therapies, from about 0.1 wt.% to about 1.0 wt.%, preferably about 0.2 wt.% of chlorhexidine, has been found to be effective. The preparations further include a non-toxic amount of at least one non-steroidal anti-inflammatory agent, most preferably indocin, ibuprofen and/or ketoprofen, in an amount ranging from about 2 wt.% to about 5 wt.% of the total preparation.

The active ingredients are incorporated into a solution, cream, rinse, lotion, gel or other acceptable carrier. In some instances, depending upon the particular carrier, the active ingredients are first solubilized and then incorporated into the carrier. The addition of a suspending agent to the carrier such as, for example, acacia powder, xanthan gum, methylcellulose, hydroxymethylcellulose or hydroxypropylcellulose, has been found to be particularly useful when compounding the carrier. In this regard, hydroxymethylcellulose gel is the preferred carrier where treatment requires manual application of the preparation to affected epidermal or muco-epidermal tissue.

Example I

Ten patients exhibiting advanced periodontal disease were treated with a preparation of 0.2% chlorhexidine and 2% ketoprofen incorporated into a

hydroxymethylcellulose gel. The patients were each instructed to apply one of the preparations to the affected gums with a tooth brush twice a day for a week. All of these patients experienced relief from pain, infection and inflammation after the prescribed course of therapy.

Example II

Two surgical patients were instructed to apply the preparation described in Example I to post surgical sites twice a day for seven days. In both cases pain, inflammation and infection at the affected sites were relieved.

Example III

Three patients exhibiting acne sores were instructed to apply the preparation described in Example I to the affected sites twice a day for seven days. In all cases, treatment with the preparations provided a reduction in the pain and inflammation associated with the sores.

Example IV

One patient undergoing radiation therapy and two patients undergoing chemotherapy were each instructed to apply the preparation described in Example I twice daily for one week. All three patients received relief from pain and showed faster healing rates of intraoral tissues following treatment with the prescribed preparations.

While preferred embodiments have been shown and described, various modifications and substitutions may be made without departing from the spirit and scope of the invention. For example, those skilled in the art will recognize that related derivatives of the active ingredients, such as pharmaceutically acceptable salts of chlorhexidine, and other prostaglandin inhibitors, such as flurbiprofen and naproxen, are useful in practicing the present invention

I Claim:

1. A topical pharmaceutical preparation for the treatment of epidermal and muco-epidermal tissue comprising a therapeutic amount of chlorhexidine and a non-toxic amount of at least one non-steroidal anti-inflammatory agent.

2. The topical preparation of claim 1 wherein the non-steroidal anti-inflammatory agent is a prostaglandin inhibitor.

3. The topical preparation of claim 1 wherein the non-steroidal anti-inflammatory agent is a prostaglandin inhibitor selected from the group consisting of indocin, ibuprofen, ketoprofen, flurbiprofen, naproxen and mixtures thereof.

4. The topical preparation of claim 1 wherein chlorhexidine is present in an amount ranging from about 0.1 wt.% to about 1.0 wt.% of the total preparation.

5. The topical preparation of claim 1 wherein the non-steroidal anti-inflammatory agent is present in an amount ranging from about 2 wt.% to about 5 wt.% of the total preparation.

6. The topical preparation of claim 1 wherein the preparation further comprises a pharmaceutical carrier incorporating the chlorhexidine and the non-steroidal anti-inflammatory agent.

7. The topical preparation of claim 6 wherein the carrier is selected from the group consisting of a solution, cream, rinse, lotion and gel.

8. A topical pharmaceutical preparation for the treatment of epidermal and muco-epidermal tissue comprising a therapeutic amount of chlorhexidine and at least one non-steroidal anti-inflammatory agent selected from the group consisting of indocin, ibuprofen, ketoprofen and mixtures thereof incorporated into a pharmaceutical carrier.

9. The topical preparation of claim 8 wherein the chlorhexidine is present in an amount ranging from about 0.1 wt.% to about 1.0 wt.% and the non-steroidal anti-inflammatory agent is present in an amount ranging from about 2 to about 5 wt.%.

10. The topical pharmaceutical preparation of claim 9 wherein the carrier is a gel.

11. A method for the treatment of epidermal and muco-epidermal tissue, said method comprising the steps of:

providing a topical pharmaceutical preparation including a carrier incorporating a therapeutic amount of chlorhexidine and a non-toxic amount of at least one non-steroidal anti-inflammatory agent, and

applying the preparation directly to epidermal and muco-epidermal tissue having pain, inflammation, infection or lesion associated therewith.

12. The method of claim 11 further characterized in that the non-steroidal anti-inflammatory agent is a prostaglandin inhibitor selected from the group consisting of indocin, ibuprofen, ketoprofen, flurbiprofen, naproxen and mixtures thereof.

13. The method of claim 11 further characterized in that the chlorhexidine is present in an amount ranging from about 0.1 wt.% to about 1.0 wt.% and the non-steroidal anti-inflammatory agent is present in an amount ranging from about 2 to about 5 wt.%.

14. The method of claim 11 further characterized in that the carrier is selected from the group consisting of a solution, cream, rinse, lotion and gel.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US94/08944

A. CLASSIFICATION OF SUBJECT MATTER

IPC(5) :A61K 7/44
US CL : 424/60

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 424/60

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

none

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

APS, MEDLINE, CAS ONLINE, DERWENT

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US, A, 4,767,751 (Davis) 30 August 1988, see entire Document.	1-14
Y	US, A, 4,975,271 (Dunn et al) 04 December 1990, see entire Document.	1-14
Y	US, A, 4,789,667 (Makino et al) 06 December 1988, see entire Document.	1-14
Y	US, A, 4,814,176 (Makino et al) 21 March 1989, see entire Document.	1-14
Y	US, A, 5,102,666 (Acharya) 07 April 1992, see entire Document.	1-14
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[X] Further documents are listed in the continuation of Box C. [ ] See patent family annex.

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INTERNATIONAL SEARCH REPORT

International application No.
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C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US, A, 4,740,365 (Yukimatsu et al) 26 April 1988, see entire Document.	1-14
Y	US, A, 4,906,670 (Higashi et al) 06 March 1990, see entire Document.	1-14